

FILE 'HCAPLUS' ENTERED AT 12:31:11 ON 12 AUG 2001

FILE 'REGISTRY' ENTERED AT 12:31:13 ON 12 AUG 2001

L115 79 S L8 NOT L16,L50  
L116 .77 S L115 NOT (PMS/CI OR C17H18N2O6)

FILE 'HCAPLUS' ENTERED AT 12:32:41 ON 12 AUG 2001

L117 220938 S L116  
L118 7454 S L117 AND L67  
L119 7454 S L118 AND L21-L25  
L120 24 S L119 AND L50 (L) THU/RL  
L121 4 S L120 AND L29  
L122 9 S L107,L20,L121  
L123 4 S L120,L114 AND L122  
L124 22 S L120,L114 NOT L122  
L125 3 S L124 AND (SYNERG? OR COMBINED TREATMENT)  
L126 9 S L122,L123  
L127 9 S L126 AND L1-L6,L19-L35,L51-L56,L60-L114,L117-L125  
L128 9 S L127 AND L19  
L129 5 S L127 AND L50  
L130 5 S L127 AND L33  
L131 5 S L129,L130  
L132 4 S L128 NOT L131  
L133 9 S L131,L132

FILE 'REGISTRY' ENTERED AT 12:40:26 ON 12 AUG 2001

FILE 'HCAPLUS' ENTERED AT 12:41:08 ON 12 AUG 2001

FILE 'WPIX' ENTERED AT 12:41:23 ON 12 AUG 2001

E AOMATSU A/AU  
L134 2 S E3  
E A61K031-195/IC, ICM, ICS  
L135 3157 S E3-E5  
L136 76 S A61P025/IC, ICM, ICS, ICA, ICI AND L135  
L137 2 S L136 AND AMINO (S) BUTANOIC  
L138 13 S L135 AND AMINO (S) BUTANOIC  
L139 1 S L135 AND AMINO (S) BUTANOATE  
L140 14 S L137-L139  
L141 7 S L140 AND 4 AMINO 3  
L142 7 S L134,L141  
L143 6 S L135 AND 4 AMINOBUTYRIC  
L144 1 S L135 AND 4 AMINOBUTANO?  
L145 6 S L143,L144  
L146 12 S L142,L145  
L147 3 S L135 AND 4 AMINO BUT?  
L148 13 S L146,L147  
L149 3 S M782/M0,M1,M2,M3,M4,M5,M6 AND L148  
L150 120 S L33  
L151 3 S L148 AND L150  
L152 5 S L149,L151  
E GABAPENTIN/DCN  
E E3+ALL  
L153 . 53 S E2  
E PREGABALIN/DCN  
E BACLOFEN/DCN  
E E4+ALL  
L154 29 S E2  
L155 2 S BACLOPHEN?  
L156 2 S L153-L155 AND L148  
L157 5 S L152,L156

FILE 'WPIX' ENTERED AT 12:57:53 ON 12 AUG 2001

L57 7 S L36 NOT L50  
 L58 1 S L57 AND C4H9NO2  
 L59 6 S L57 NOT L58

FILE 'HCAPLUS' ENTERED AT 11:53:39 ON 12 AUG 2001

L60 5 S L59  
 L61 4 S L59 AND L32  
 L62 1 S L60 NOT L61  
 L63 15 S L56,L61  
 L64 389 S L58/D  
 L65 7 S L64 AND L32  
 L66 35 S L32,L63,L65  
 L67 21856 S L19,L51,L64 AND (PD<=19980515 OR PRD<=19980518 OR AD<=1998051  
 L68 421 S L16 (L) THU/RL AND L67  
 L69 187 S L68 AND L21-L25  
 L70 20 S L68 AND L26  
 L71 18 S L68 AND L28  
 L72 25 S L70,L71  
 L73 10 S L72 AND L33,L51  
 L74 7 S L72 AND L63  
 L75 3 S L73 NOT L74  
 L76 623 S L67 AND (STABLE OR UNSTABLE OR STABIL? OR INSTABIL?)  
 L77 4 S L76 AND L66  
 E STAB/CT  
 E E12+ALL  
 L78 4819 S E3  
 E E25+ALL  
 L79 72624 S E2+NT  
 E E22+ALL  
 L80 66439 S E2+NT  
 E E17+ALL  
 L81 8534 S E1+NT  
 L82 253 S E14+NT  
 L83 5598 S E17+NT  
 L84 54 S L67 AND L78-L83  
 L85 19 S L84 AND AMINO ACID?/CT  
 L86 48 S L84 AND L21-L26  
 L87 13 S L84 AND L28  
 L88 3 S L84 AND L31  
 L89 8 S L84 AND L33  
 L90 8 S L84 AND L51  
 L91 49 S L85-L90  
 L92 3 S L91 AND L72  
 L93 1 S L92 AND L64  
 L94 93 S L20,L32,L66,L72-L75,L77,L91-L93  
 L95 20 S L94 AND 63/SC  
 L96 46 S L94 AND (COMPOSITION OR COMBIN? OR MIX? OR SYNERG? OR CONCOMI  
 L97 34 S L96 AND (1 OR 63)/SC,SX  
 L98 29 S L96 AND THU/RL  
 L99 36 S L97,L98  
 L100 16 S L94 AND (?COMPLEX? OR ?CONJUGAT?)  
 L101 41 S L99,L100  
 L102 30 S L101 AND AMINO ACID?/CT  
 L103 11 S L101 NOT L102  
 L104 8 S L102 AND STAB?  
 L105 22 S L102 NOT L104  
 L106 7 S L105 AND (MODIFIED OR AGONIST OR IMPROVED OR TOPICAL OR SUGAR  
 SEL DN 6 7  
 L107 5 S L106 NOT E1-E2  
 L108 1774 S L51 AND L67  
 L109 263 S L108 AND L68  
 L110 263 S L50 (L) THU/RL AND L109  
 L111 6 S L26 AND L110  
 L112 6 S L29 AND L110  
 L113 6 S L111,L112  
 L114 6 S L113 AND L21-L25

FILE 'REGISTRY' ENTERED AT 11:24:49 ON 12 AUG 2001

L7 104 S E1-E104  
L8 89 S L7 AND N/ELS  
L9 STR  
L10 2 S L9  
L11 SCR 1568 AND 1312  
L12 4 S L9 AND L11  
L13 SCR 1007  
L14 2 S L9 AND L11 AND L13  
L15 2 S L12 NOT L14  
L16 1165 S L9 AND L11 FUL  
SAV L16 KWON674/A  
L17 10 S L7 AND L16  
L18 94 S L7 NOT L17

FILE 'HCAPLUS' ENTERED AT 11:31:47 ON 12 AUG 2001

L19 24235 S L16  
L20 3 S L6 AND L19  
E AMINO ACID/CT  
E E61+NT  
L21 22136 S E1-E50 AND L19  
L22 1322 S E51-E100 AND L19  
L23 8324 S E101-E150 AND L19  
L24 2958 S E151-E200 AND L19  
L25 292 S E201-E222 AND L19  
E AMINO ACIDS/CT  
L26 2066 S AMINO ACIDS/CT (L) THU/RL  
L27 49 S L26 AND L21-L25  
E AMINO ACIDS, BIOLOGICAL STUDIES/CT  
L28 3298 S E3 AND L19  
L29 30 S E3(L)THU/RL AND L19  
L30 49 S L27,L29  
L31 49 S L21-L29 AND L30  
L32 35 S L31 AND (1 OR 63)/SC, SX  
L33 3505 S GABAPENTIN? OR PREGABALIN? OR BACLOFEN?  
L34 0 S 3() (AMINOMETHYL OR AMINO METHYL) () 4() (CYCLOHEXYL OR CYCLO HEX  
L35 0 S 3() (AMINOMETHYL OR AMINO METHYL) () 4() (CYCLOHEXYLBUTANOIC OR C  
SEL HIT RN L20

FILE 'REGISTRY' ENTERED AT 11:45:32 ON 12 AUG 2001

L36 10 S E1-E10  
L37 3 S 1134-47-0 OR 60142-96-3 OR 148553-50-8  
L38 7 S L36 NOT L37  
L39 6 S L38 AND C6/ES  
L40 3 S L39 AND 46.150.1/RID  
L41 3 S L39 NOT L40  
L42 6 S C8H17NO2/MF AND L16  
L43 3 S L42 AND HEXANOIC AND 5  
L44 5 S L37,L43  
L45 12 S L16 AND C10H12CLNO2/MF  
L46 9 S L45 AND BENZENEPANOIC AND 4 CHLORO  
L47 3 S L46 NOT (11C# OR 13C# OR 14C# OR LABELED OR (D OR T)/ELS)  
L48 34 S L16 AND C9H17NO2/MF  
L49 2 S L48 AND 46.150.1/RID  
L50 7 S L37,L44,L47

FILE 'HCAPLUS' ENTERED AT 11:51:48 ON 12 AUG 2001

L51 2191 S L50  
L52 13 S L51 AND L32  
L53 13 S L33 AND L32  
L54 14 S L52,L53  
L55 3 S L20 AND L51,L32,L33  
L56 14 S L54,L55

FILE 'REGISTRY' ENTERED AT 11:52:57 ON 12 AUG 2001

=> fil reg  
FILE 'REGISTRY' ENTERED AT 12:40:26 ON 12 AUG 2001  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2001 American Chemical Society (ACS)

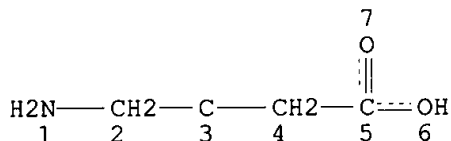
STRUCTURE FILE UPDATES: 10 AUG 2001 HIGHEST RN 351153-64-5  
DICTIONARY FILE UPDATES: 10 AUG 2001 HIGHEST RN 351153-64-5

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT  
for details.

=> d sta que l16  
L9 STR



NODE ATTRIBUTES:  
NSPEC IS RC AT 3  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE  
L11 SCR 1568 AND 1312  
L16 1165 SEA FILE=REGISTRY SSS FUL L9 AND L11

100.0% PROCESSED 238676 ITERATIONS  
SEARCH TIME: 00.00.09

Point of Contact:  
Jan Delav  
Librarian-Physical Sciences  
CM1 1E01 Tel: 308-4498

*1. Gabapentin (pregabalin)*

1165 ANSWERS

=> d ide can tot 150

L50 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2001 ACS  
RN 148553-51-9 REGISTRY  
CN Hexanoic acid, 3-(aminomethyl)-5-methyl-, (3R)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:  
CN Hexanoic acid, 3-(aminomethyl)-5-methyl-, (R)-  
OTHER NAMES:

CN (R)-Pregabalin

CN PD 144550

FS STEREOSEARCH

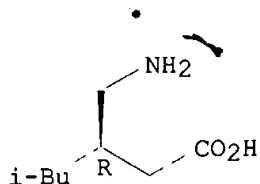
MF C8 H17 N O2

CI COM

SR CA

LC STN Files: BEILSTEIN\*, CA, CAPLUS, DRUGUPDATES, TOXLIT, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



13 REFERENCES IN FILE CA (1967 TO DATE)  
13 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:320768  
REFERENCE 2: 134:125863  
REFERENCE 3: 132:274197  
REFERENCE 4: 132:102843  
REFERENCE 5: 131:97392  
REFERENCE 6: 130:191891  
REFERENCE 7: 130:191890  
REFERENCE 8: 130:90504  
REFERENCE 9: 129:156883  
REFERENCE 10: 129:62851

L50 ANSWER 2 OF 7 REGISTRY. COPYRIGHT 2001 ACS

RN 148553-50-8 REGISTRY

CN Hexanoic acid, 3-(aminomethyl)-5-methyl-, (3S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Hexanoic acid, 3-(aminomethyl)-5-methyl-, (S)-

OTHER NAMES:

CN CI 1008

CN PD 144723

CN Pregabalin

FS STEREOSEARCH

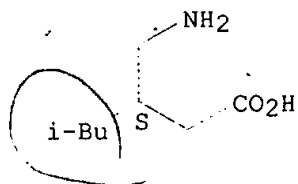
MF C8 H17 N O2

CI COM

SR CA

LC STN Files: ADISINSIGHT, BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MRCK\*, PHAR, PROMT, SYNTHLINE, TOXLINE, TOXLIT, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (+).

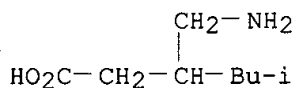


61 REFERENCES IN FILE CA (1967 TO DATE)  
62 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:101698  
REFERENCE 2: 135:66248

REFERENCE 3: 135:24671  
 REFERENCE 4: 134:331617  
 REFERENCE 5: 134:320768  
 REFERENCE 6: 134:285590  
 REFERENCE 7: 134:271290  
 REFERENCE 8: 134:202706  
 REFERENCE 9: 134:198075  
 REFERENCE 10: 134:131540

L50 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2001 ACS  
 RN 128013-69-4 REGISTRY  
 CN **Hexanoic acid, 3-(aminomethyl)-5-methyl- (9CI)** (CA INDEX NAME)  
 FS 3D CONCORD  
 DR 130912-52-6  
 MF **C8 H17 N O2**  
 SR CA  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, DRUGUPDATES, SYNTHLINE,  
 TOXLIT, USPATFULL  
 (\*File contains numerically searchable property data)



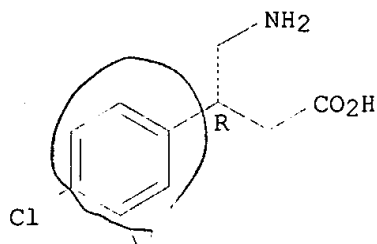
8 REFERENCES IN FILE CA (1967 TO DATE)  
 8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:288785  
 REFERENCE 2: 131:58836  
 REFERENCE 3: 130:38664  
 REFERENCE 4: 128:149590  
 REFERENCE 5: 126:104423  
 REFERENCE 6: 126:103837  
 REFERENCE 7: 118:182788  
 REFERENCE 8: 113:41285

L50 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2001 ACS  
 RN 69308-37-8 REGISTRY  
 CN **Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro-, (.beta.R)- (9CI)** (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN **Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro-, (R)-**  
 OTHER NAMES:  
 CN (-)-Baclofen  
 CN (R)-(-)-Baclofen  
 CN **(R)-4-Amino-3-(4-chlorophenyl)butanoic acid**  
 CN (R)-Baclofen  
 CN D-Baclofen  
 CN l-Baclofen  
 CN R-(-)-Baclofen

FS STEREOSEARCH  
 MF C10 H12 Cl N O2  
 CI COM  
 LC STN Files: ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, CA, CAPLUS,  
 CASREACT, CEN, CHEMCATS, PROMT, TOXLIT, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



187 REFERENCES IN FILE CA (1967 TO DATE)  
 187 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:306509  
 REFERENCE 2: 134:231440  
 REFERENCE 3: 134:142141  
 REFERENCE 4: 134:141758  
 REFERENCE 5: 133:329945  
 REFERENCE 6: 133:305526  
 REFERENCE 7: 133:183136  
 REFERENCE 8: 133:177033  
 REFERENCE 9: 133:172447  
 REFERENCE 10: 132:202993

L50 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2001 ACS  
 RN 66514-99-6 REGISTRY  
 CN Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro-, (.beta.S)-  
 (9CI) (CA INDEX NAME)

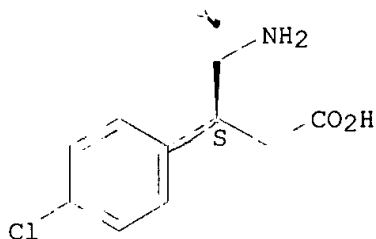
OTHER CA INDEX NAMES:

CN Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro-, (S)-

OTHER NAMES:

CN (+)-Baclofen  
 CN (S)-4-Amino-3-(4-chlorophenyl)butanoic acid  
 CN (S)-Baclofen  
 CN d-Baclofen  
 CN L-(+)-Baclofen  
 CN L-Baclofen  
 CN S(+)-Baclofen  
 FS STEREOSEARCH  
 MF C10 H12 Cl N O2  
 CI COM  
 LC STN Files: ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS, CA, CAPLUS,  
 CASREACT, CEN, TOXLIT, USPATFULL  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



222 REFERENCES IN FILE CA (1967 TO DATE)  
222 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:290661  
REFERENCE 2: 134:231440  
REFERENCE 3: 133:217711  
REFERENCE 4: 133:183136  
REFERENCE 5: 131:299661  
REFERENCE 6: 131:284829  
REFERENCE 7: 131:252676  
REFERENCE 8: 131:237936  
REFERENCE 9: 131:157932  
REFERENCE 10: 131:139952

L50 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2001 ACS

RN 60142-96-3 REGISTRY

CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1-(Aminomethyl)cyclohexaneacetic acid

CN CI 945

CN Gabapentin

CN Go 3450

CN GOE 2450

CN Neurontin

FS 3D CONCORD

MF C9 H17 N O2

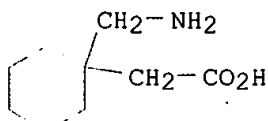
CI COM

LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN\*,  
BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB,  
CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU,  
DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE,  
MRCK\*, MSDS-OHS, PHAR, PROMT, RTECS\*, SYNTHLINE, TOXLINE, TOXLIT, USAN,  
USPATFULL

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)



447 REFERENCES IN FILE CA (1967 TO DATE)



18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
151 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:111992  
REFERENCE 2: 135:105918  
REFERENCE 3: 135:102395  
REFERENCE 4: 135:102372  
REFERENCE 5: 135:101700  
REFERENCE 6: 135:97445  
REFERENCE 7: 135:87387  
REFERENCE 8: 135:87084  
REFERENCE 9: 135:87018  
REFERENCE 10: 135:86988

L50 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2001 ACS

RN 1134-47-0 REGISTRY

CN Benzenepropanoic acid, .beta.-(aminomethyl)-4-chloro- (9CI) (CA  
INDEX NAME)

OTHER CA INDEX NAMES:

CN Hydrocinnamic acid, .beta.-(aminomethyl)-p-chloro- (7CI, 8CI)

OTHER NAMES:

CN (.+-.)-Baclofen

CN .beta.-(4-Chlorophenyl)-.gamma.-aminobutyric acid

CN .beta.-(Aminomethyl)-p-chlorohydrocinnamic acid

CN .beta.-(p-Chlorophenyl)-.gamma.-aminobutyric acid

CN .beta.-p-Chlorophenyl-GABA

CN 4-Amino-3-(4-chlorophenyl)butyric acid

CN 4-Amino-3-(p-chlorophenyl)butyric acid

CN Ba 34647

CN Baclofen

CN C 34647Ba

CN CIBA Ba 34647

CN DL-4-Amino-3-p-chlorophenylbutanoic acid

CN DL-Baclofen

CN dl-Baclofen

CN Lioresal

FS 3D CONCORD

DR 62594-36-9

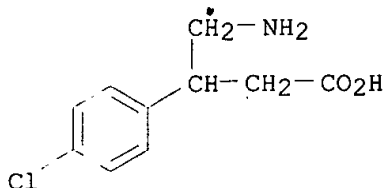
MF C10 H12 Cl N O2

CI COM

LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,  
CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, IFICDB,  
IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC,  
PROMT, RTECS\*, SPECINFO, SYNTHLINE, TOXLINE, TOXLIT; USAN, USPATFULL  
(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)



1364 REFERENCES IN FILE CA (1967 TO DATE)

36 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1366 REFERENCES IN FILE CAPLUS (1967 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:111958  
 REFERENCE 2: 135:102802  
 REFERENCE 3: 135:102657  
 REFERENCE 4: 135:55467  
 REFERENCE 5: 135:44168  
 REFERENCE 6: 135:41034  
 REFERENCE 7: 135:29335  
 REFERENCE 8: 135:28954  
 REFERENCE 9: 135:24671  
 REFERENCE 10: 135:17656

=> d his

(FILE 'HOME' ENTERED AT 11:22:43 ON 12 AUG 2001)  
 SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:22:57 ON 12 AUG 2001  
 E WO9959573/PN

L1 1 S E3  
 E WO99-US10190/AP, PRN  
 L2 1 S E3, E4  
 E JP98-133113/AP, PRN  
 L3 1 S E4  
 L4 1 S L1-L3  
 E AOMATSU A/AU  
 L5 4 S E4  
 L6 4 S L4, L5  
 SEL RN

FILE 'REGISTRY' ENTERED AT 11:24:49 ON 12 AUG 2001

L7 104 S E1-E104  
 L8 89 S L7 AND N/ELS  
 L9 STR  
 L10 2 S L9  
 L11 SCR 1568 AND 1312  
 L12 4 S L9 AND L11  
 L13 SCR 1007  
 L14 2 S L9 AND L11 AND L13  
 L15 2 S L12 NOT L14  
 L16 1165 S L9 AND L11 FUL  
 SAV L16 KWON674/A

L17 10 S L7 AND L16  
L18 94 S L7 NOT L17

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L19 24235 S L16  
L20 3 S L6 AND L19  
E AMINO ACID/CT  
E E61+NT  
L21 22136 S E1-E50 AND L19  
L22 1322 S E51-E100 AND L19  
L23 8324 S E101-E150 AND L19  
L24 2958 S E151-E200 AND L19  
L25 292, S E201-E222 AND L19  
E AMINO ACIDS/CT  
L26 2066 S AMINO ACIDS/CT (L) THU/RL  
L27 49 S L26 AND L21-L25  
E AMINO ACIDS, BIOLOGICAL STUDIES/CT  
L28 3298 S E3 AND L19  
L29 30 S E3(L)THU/RL AND L19  
L30 49 S L27,L29  
L31 49 S L21-L29 AND L30  
L32 35 S L31 AND (1 OR 63)/SC, SX  
L33 3505 S GABAPENTIN? OR PREGABALIN? OR BACLOFEN?  
L34 0 S 3() (AMINOMETHYL OR AMINO METHYL) () 4() (CYCLOHEXYL OR CYCLO HEX  
L35 0 S 3() (AMINOMETHYL OR AMINO METHYL) () 4() (CYCLOHEXYLBUTANOIC OR C  
SEL HIT RN L20

FILE 'REGISTRY' ENTERED AT 11:45:32 ON 12 AUG 2001

L36 10 S E1-E10  
L37 3 S 1134-47-0 OR 60142-96-3 OR 148553-50-8  
L38 7 S L36 NOT L37  
L39 6 S L38 AND C6/ES  
L40 3 S L39 AND 46.150.1/RID  
L41 3 S L39 NOT L40  
L42 6 S C8H17NO2/MF AND L16  
L43 3 S L42 AND HEXANOIC AND 5  
L44 5 S L37,L43  
L45 12 S L16 AND C10H12CLNO2/MF  
L46 9 S L45 AND BENZENEPROPANOIC AND 4 CHLORO  
L47 3 S L46 NOT (11C# OR 13C# OR 14C# OR LABELED OR (D OR T)/ELS)  
L48 34 S L16 AND C9H17NO2/MF  
L49 2 S L48 AND 46.150.1/RID  
L50 7 S L37,L44,L47

FILE 'HCAPLUS' ENTERED AT 11:51:48 ON 12 AUG 2001

L51 2191 S L50  
L52 13 S L51 AND L32  
L53 13 S L33 AND L32  
L54 14 S L52,L53  
L55 3 S L20 AND L51,L32,L33  
L56 14 S L54,L55

FILE 'REGISTRY' ENTERED AT 11:52:57 ON 12 AUG 2001

L57 7 S L36 NOT L50  
L58 1 S L57 AND C4H9NO2  
L59 6 S L57 NOT L58

FILE 'HCAPLUS' ENTERED AT 11:53:39 ON 12 AUG 2001

L60 5 S L59  
L61 4 S L59 AND L32  
L62 1 S L60 NOT L61  
L63 15 S L56,L61  
L64 389 S L58/D  
L65 7 S L64 AND L32  
L66 35 S L32,L63,L65  
L67 21856 S L19,L51,L64 AND (PD<=19980515 OR PRD<=19980518 OR AD<=1998051

L68 421 S L16 (L) THU/RL AND L67  
 L69 187 S L68 AND L21-L25  
 L70 20 S L68 AND L26  
 L71 18 S L68 AND L28  
 L72 25 S L70, L71  
 L73 10 S L72 AND L33, L51  
 L74 7 S L72 AND L63  
 L75 3 S L73 NOT L74  
 L76 623 S L67 AND (STABLE OR UNSTABLE OR STABIL? OR INSTABIL?)  
 L77 4 S L76 AND L66  
     E STAB/CT  
     E E12+ALL  
 L78 4819 S E3  
     E E25+ALL  
 L79 72624 S E2+NT  
     E E22+ALL  
 L80 66439 S E2+NT  
     E E17+ALL  
 L81 8534 S E1+NT  
 L82 253 S E14+NT  
 L83 5598 S E17+NT  
 L84 54 S L67 AND L78-L83  
 L85 19 S L84 AND AMINO ACID?/CT  
 L86 48 S L84 AND L21-L26  
 L87 13 S L84 AND L28  
 L88 3 S L84 AND L31  
 L89 8 S L84 AND L33  
 L90 8 S L84 AND L51  
 L91 49 S L85-L90  
 L92 3 S L91 AND L72  
 L93 1 S L92 AND L64  
 L94 93 S L20, L32, L66, L72-L75, L77, L91-L93  
 L95 20 S L94 AND 63/SC  
 L96 46 S L94 AND (COMPOSITION OR COMBIN? OR MIX? OR SYNERG? OR CONCOMI  
 L97 34 S L96 AND (1 OR 63)/SC, SX  
 L98 29 S L96 AND THU/RL  
 L99 36 S L97, L98  
 L100 16 S L94 AND (?COMPLEX? OR ?CONJUGAT?)  
 L101 41 S L99, L100  
 L102 30 S L101 AND AMINO ACID?/CT  
 L103 11 S L101 NOT L102  
 L104 8 S L102 AND STAB?  
 L105 22 S L102 NOT L104  
 L106 7 S L105 AND (MODIFIED OR AGONIST OR IMPROVED OR TOPICAL OR SUGAR  
     SEL DN 6 7  
 L107 5 S L106 NOT E1-E2  
 L108 1774 S L51 AND L67  
 L109 263 S L108 AND L68  
 L110 263 S L50 (L) THU/RL AND L109  
 L111 6 S L26 AND L110  
 L112 6 S L29 AND L110  
 L113 6 S L111, L112  
 L114 6 S L113 AND L21-L25

FILE 'HCAPLUS' ENTERED AT 12:31:11 ON 12 AUG 2001

FILE 'REGISTRY' ENTERED AT 12:31:13 ON 12 AUG 2001

L115 79 S L8 NOT L16, L50  
 L116 77 S L115 NOT (PMS/CI OR C17H18N2O6)

FILE 'HCAPLUS' ENTERED AT 12:32:41 ON 12 AUG 2001

L117 220938 S L116  
 L118 7454 S L117 AND L67  
 L119 7454 S L118 AND L21-L25  
 L120 24 S L119 AND L50 (L) THU/RL  
 L121 4 S L120 AND L29

L122 9 S L107,L20,L121  
 L123 4 S L120,L114 AND L122  
 L124 22 S L120,L114 NOT L122  
 L125 3 S L124 AND (SYNERG? OR COMBINED TREATMENT)  
 L126 9 S L122,L123  
 L127 9 S L126 AND L1-L6,L19-L35,L51-L56,L60-L114,L117-L125  
 L128 9 S L127 AND L19  
 L129 5 S L127 AND L50  
 L130 5 S L127 AND L33  
 L131 5 S L129,L130  
 L132 4 S L128 NOT L131  
 L133 9 S L131,L132

FILE 'REGISTRY' ENTERED AT 12:40:26 ON 12 AUG 2001

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 12:41:08 ON 12 AUG 2001  
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FILE COVERS 1947 - 12 Aug 2001 VOL 135 ISS 8  
 FILE LAST UPDATED: 10 Aug 2001 (20010810/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCaplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

=> d bib abs hitrn tot l133

L133 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2000:608551 HCAPLUS  
 DN 133:213151  
 TI Pharmaceutical **compositions** and methods for **improved**  
 delivery of hydrophobic therapeutic agents  
 IN Patel, Manesh V.; Chen, Feng-Jing  
 PA Lipocine, Inc., USA  
 SO PCT Int. Appl., 98 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000050007	A1	20000831	WO 2000-US165	20000105
	W:				
	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,				
	CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,				
	IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,				
	MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,				
	SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,				

BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-258654 A 19990226

AB The present invention relates to triglyceride-free pharmaceutical **compns.** for delivery of hydrophobic therapeutic agents. **Compns.** of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a **combination** of a hydrophilic surfactant and a hydrophobic surfactant. Upon diln. with an aq. solvent, the **compn.** forms a clear, aq. dispersion of the surfactants contg. the therapeutic agent. The invention also provides methods of treatment with hydrophobic therapeutic agents using these **compns.** A pharmaceutical **compn.** contained cyclosporin 0.14, Cremophor RH-40 0.41, Arlacell186 0.29, sodium taurocholate 0.26, and propylene glycol 0.46 mg.

IT 51-48-9, L-Thyroxine, biological studies 1134-47-0, Baclofen 60142-96-3, Gabapentin  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical **compns.** and methods for improved delivery of hydrophobic therapeutic agents)

RE.CNT 4

RE

- (1) Crooks; US 4572915 A 1986 HCAPLUS
- (2) Muller; US 4719239 A 1988 HCAPLUS
- (3) Schmidt; US 4727109 A 1988 HCAPLUS
- (4) Story; US 4944949 A 1990 HCAPLUS

L133 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:80040 HCAPLUS

DN 132:127733

TI **Stabilized** solid preparations of 4-amino-3-substituted-butanoic acid derivatives and their manufacture

IN Aomatsu, Akira

PA Warner Lambert Co., USA

SO Jpn. Kokai Tokkyo Koho, 34 pp.  
 CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2000034227	A2	20000202	JP 1999-133769	19990514 <--
PRAI	JP 1998-133112	A	19980515	<--	
OS	MARPAT 132:127733				

AB Solid preps. of H<sub>2</sub>NCH<sub>2</sub>CR<sub>1</sub>R<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H [I; R<sub>1</sub> = H, OH, Me, Et; R<sub>2</sub> = various (un)substituted hydrocarbyl (definitions are described in detail)], useful as nervous system agents for treatment of epilepsy, syncope, head trauma, cerebral dysfunction, Alzheimer disease, Huntington chorea, parkinsonism, etc., are manufd. by adding water-holding agents such as ethylene glycol, propylene glycol, glycerin, etc., and optionally excipients. The preps. may addnl. contain neutral amino acids. Water-holding agents prevents deterioration of I due to lactam formation. Gabapentin was spray-coated with an aq. propylene glycol soln. to give powder contg. 0.003% lactam. The powder was stored in a sealed container at -60 degree. for 2 wk to show lactam content 0.011%, vs. 0.017% for control powder contg. no propylene glycol.

IT ~~56-40-6~~, Glycine, biological studies 56-41-7, L-Alanine, biological studies 61-90-5, L-Leucine, biological studies 72-18-4, L-Valine, biological studies 73-32-5, L-Isoleucine, biological studies 302-72-7, Alanine 319-78-8, D-Isoleucine 328-38-1, D-Leucine 328-39-2, Leucine 338-69-2, D-Alanine 443-79-8, Isoleucine 516-06-3, Valine 640-68-6, D-Valine  
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**stabilization** of solid preps. of 4-amino-3-substituted-butanoic acid derivs. as nervous system agents by addn. of water-holding agents)

IT 1134-47-0, Baclofen 30200-05-6  
60142-96-3, Gabapentin 148553-50-8,  
Pregabalin 206749-40-8 256418-06-1  
256418-07-2

RL: THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)  
(**stabilization** of solid preps. of 4-amino-3-substituted-butanoic acid derivs. as nervous system agents by addn. of water-holding agents)

L133 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:753061 HCAPLUS

DN 132:6349

TI Preparation of **stabilized** pharmaceuticals containing .gamma.-aminobutyric acid derivatives

IN Aomatsu, Akira

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 115 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959573	A1	19991125	WO 1999-US10190	19990510 <--
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9940735	A1	19991206	AU 1999-40735	19990510 <--
	BR 9910508	A	20010102	BR 1999-10508	19990510 <--
	EP 1077692	A1	20010228	EP 1999-924166	19990510 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2000005768	A	20001114	NO 2000-5768	20001114 <--
PRAI	JP 1998-133113	A	19980515 <--		
	WO 1999-US10190	W	19990510 <--		

OS MARPAT 132:6349

AB The present invention provides a **stabilized** pharmaceutical prepn. of a 4-amino-3-substituted butanoic acid deriv. which can be obtained by incorporating an amino acid as a **stabilizer**. Thus, a sample was prepd. by dissolving 500 mg of **gabapentin** crystals in water to make up a total vol. of 10 mL and stored under various conditions. The degrdn. of **gabapentin** stored, e.g., for 4 wk at 45.degree. was prevented by the addn. of L-valine or glycine.

IT 51-48-9, L-Thyroxine, biological studies 56-12-2D, .gamma.-Aminobutyric acid, derivs. 56-40-6, Glycine, biological studies 56-41-7, L-Alanine, biological studies 56-45-1, L-Serine, biological studies 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 56-89-3, L-Cystine, biological studies 59-92-7, Levodopa, biological studies 60-18-4, L-Tyrosine, biological studies 61-90-5, L-Leucine, biological studies 61-90-5D, L-Leucine, hydroxy derivs. 62-57-7, 2-Aminoisobutyric acid 63-68-3, L-Methionine, biological studies 63-91-2, L-Phenylalanine, biological studies 70-26-8, L-Ornithine 72-18-4, L-Valine, biological studies 72-19-5, L-Threonine, biological studies 73-22-3, L-Tryptophan, biological studies 73-22-3D, L-Tryptophan, hydroxy or Me derivs. 73-32-5, L-IsoLeucine, biological studies 73-32-5D, L-Isoleucine, hydroxy

defivs. 74-79-3, L-Arginine, biological studies 156-86-5  
 , L-HomoArginine 300-38-9, 3,5-DiBromo-L-Tyrosine  
 300-39-0, 3,5-Diiodo-L-Tyrosine 302-72-7, Alanine  
 327-57-1, L-NorLeucine 372-75-8, Citrulline  
 496-93-5, L-Canaline 537-49-5, N-Methyl-L-Tyrosine  
 537-55-3, N-Acetyl-L-Tyrosine 543-38-4, L-Canavanine  
 555-30-6, L-Methyldopa 587-33-7 595-40-4,  
 L-IsoValine 626-72-2, L-HomoCystine 638-23-3  
 672-15-1, L-HomoSerine 921-52-8, Diaminosuccinic acid  
 1115-93-1, S-Propyl-L-Cysteine 1118-90-7  
 1118-90-7D, hydroxy derivs. 1134-47-0, Baclofen  
 1187-84-4, S-Methyl-L-Cysteine 1190-94-9,  
 Hydroxy-L-lysine 1492-24-6, L-2-Aminobutyric acid  
 1492-24-6D, L-2-Aminobutyric acid, derivs. 2835-06-5  
 2835-06-5D, hydroxy derivs. 4033-39-0,  
 L-2,3-Diaminopropionic acid 6152-89-2 6600-40-4,  
 L-NorValine 6600-40-4D, L-Norvaline, derivs. 6665-12-9  
 7423-93-0, 3-Chloro-L-Tyrosine 7540-67-2,  
 O-Acetyl-L-Homoserine 13073-35-3, L-Ethionine 15091-76-6  
 , N-Hydroxy-L-Alanine 16055-12-2 16354-58-8,  
 N-Acetyl-L-Serine 16804-57-2 17093-74-2,  
 N-Acetyl-L-Threonine 17268-93-8 17673-71-1,  
 O-Butyl-L-HomoSerine 18312-28-2, O-Propyl-L-HomoSerine  
 21593-77-1, S-Allyl-L-Cysteine 25148-30-5,  
 L-HomoMethionine 26630-55-7 26630-55-7D, hydroxy  
 derivs. 26911-39-7 29784-96-1 30200-05-6  
 35187-58-7 38739-13-8, 3-Bromo-L-Tyrosine  
 44902-02-5 60142-96-3, Gabapentin  
 71292-20-1 116783-26-7 148553-50-8,  
 Pregabalin 187611-96-7 189302-41-8  
 206749-40-8 206749-41-9 250653-29-3  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (prepn. of stabilized pharmaceuticals contg.  
 .gamma.-aminobutyric acid derivs.)

RE.CNT 4

RE

- (1) Ciba Geigy AG; EP 0376891 A 1990 HCAPLUS
- (2) Kigasawa, K; US 4952560 A 1990 HCAPLUS
- (3) Nitto Electric Ind Co Ltd; JP 63253022 A 1988 HCAPLUS
- (4) Warner Lambert Co; EP 0458751 A 1991 HCAPLUS

L133 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:753060 HCAPLUS

DN 131:356133

TI Solid compositions containing .gamma.-aminobutyric acid derivatives

IN Aomatsu, Akira

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 99 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959572	A1	19991125	WO 1999-US10186	19990510 <--
	W:			AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
	RW:			GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	
	AU 9940733	A1	19991206	AU 1999-40733	19990510 <--
	BR 9910494	A	20010109	BR 1999-10494	19990510 <--
	EP 1077691	A1	20010228	EP 1999-924164	19990510 <--



R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

NO 2000005765 A 20001114 NO 2000-5765 20001114 <--

PRAI JP 1998-133122 A 19980515 <--

JP 1998-133112 A 19980515 <--

WO 1999-US10186 W 19990510

OS MARPAT 131:356133

AB The present invention provides a **stabilized solid compn** . contg. a 4-amino-3-substituted-butanoic acid deriv. which can be obtained by incorporating a humectant as a **stabilizer**. Bulk powders of **gabapentin** (250 g) were sprayed with 72 g water by means of a fluidized granulator and then dried to give **gabapentin** granular powders A. A second batch of bulk powders of **gabapentin** (250 g) were sprayed with a soln. of 5 g propylene glycol in 67 g water by means of the fluidized granulator and then dried to give **gabapentin** granular powders B. The **gabapentin** granular powders A and B obtained were stored under conditions and then the lactam formed in each of the powders was detd. by HPLC. E.g., **gabapentin** bulk powders stored for 4 wk at 50.degree. and 85% humidity did not show any degrdn.

IT 56-12-2D, .gamma.-Aminobutyric acid, derivs. 56-40-6, Glycine, biological studies 56-41-7, L-Alanine, biological studies 61-90-5, L-Leucine, biological studies 72-18-4 , L-Valine, biological studies 73-32-5, L-Isoleucine, biological studies 302-72-7, Alanine 319-78-8, D-IsoLeucine 328-38-1, D-Leucine 328-39-2, Leucine 338-69-2 , D-Alanine 443-79-8, Isoleucine 516-06-3, Valine 640-68-6, D-Valine 1134-47-0, Baclofen 30200-05-6 60142-96-3, Gabapentin 148553-50-8, Pregabalin 206749-40-8 206749-41-9 250653-29-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (solid **compns.** contg. .gamma.-aminobutyric acid derivs. and humectants)

RE.CNT 4

RE

(1) Goedecke Ag; DE 3928183 A 1991 HCAPLUS

(2) Kazuo, K; US 4952560 A 1990 HCAPLUS

(3) Nitto Electric Ind Co Ltd; JP 63253022 A 1988 HCAPLUS

(4) Warner Lambert Co; EP 0458751 A 1991 HCAPLUS

L133 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:464180 HCAPLUS

DN 131:111440

TI Methods using agents **simultaneously** acting as NMDA-type glutamate receptor antagonists and GABA-A receptor **agonists** for treating tardive dyskinesia and other movement disorders

IN Fogel, Barry S.

PA Synchroneuron, LLC, USA

SO PCT Int. Appl., 106 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9936064	A2	19990722	WO 1999-US144	19990113 <--
	WO 9936064	A3	19991202		
	W: AU, CA, CH, CN, JP, MX, NZ				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5952389	A	19990914	US 1998-6641	19980113 <--
	US 6057373	A	20000502	US 1999-224829	19990104 <--
	AU 9921041	A1	19990802	AU 1999-21041	19990113 <--
	EP 1047436	A2	20001102	EP 1999-901314	19990113 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI  
 WO 2000Q28999 A2 20000525 WO 1999-US27343 19991118  
 WO 2000028999 A3 20000720  
 W: AU, CA, CH, CN, JP, MX, NZ  
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE  
 PRAI US 1998-6641 A 19980113 <--  
 US 1998-193892 A 19981118  
 US 1999-224829 A 19990104  
 US 1997-861801 A2 19970522 <--  
 WO 1999-US144 W 19990113  
 AB The invention describes treatments for movement disorders, including tardive dyskinesia and tardive dystonia, tic disorders, Tourette's syndrome, blepharospasm, and other focal dystonias. The treatments use agents that **simultaneously** act as NMDA-type glutamate receptor antagonists. Addnl., the treatments of the invention use agents that **simultaneously** act as NMDA-type glutamate receptor antagonists and GABA-A receptor agonists. Preferably, these two activities are characteristic of a single agent, e.g. acamprosate. Alternatively, sep. agents having these activities can be **combined** and administered **together**. The invention also provides a third agent that can be used in **combination** with a treatment for movement disorders, that acts as a non-competitive NMDA-receptor blocking agent or ion channel blocker that augments the effect of the primary treatment. A particularly preferred ion channel blocking agent is magnesium. Alternatively, magnesium can be administered alone for prevention and treatment of movement disorders.  
 IT 56-12-2, GABA, biological studies  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (basal ganglia deficiency; agents **simultaneously** acting as NMDA-type glutamate receptor antagonists and GABA-A receptor agonists for treatment of movement disorders)  
 IT 6384-92-5, NMDA  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (excitotoxicity; agents **simultaneously** acting as NMDA-type glutamate receptor antagonists and GABA-A receptor agonists for treatment of movement disorders)

L133 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:219944 HCAPLUS

DN 130:242159

TI **topical** cosmetic or pharmaceutical **compositions**

**comprising** an anti-stinging effective amount of an amino acid

IN Muizzuddin, Neelam; Marenus, Kenneth D.; Rein, Glen; Matsui, Mary Steidl

PA E-L Management Corp., USA

SO PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9913819	A2	19990325	WO 1998-US19720	19980921 <--
	WO 9913819	A3	19990603		
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5958976	A	19990928	US 1997-933571	19970919 <--
	AU 9894984	A1	19990405	AU 1998-94984	19980921 <--
	EP 957887	A2	19991124	EP 1998-948404	19980921 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001505590	T2	20010424	JP 1999-518281	19980921 <--
PRAI	US 1997-933571	A	19970919 <--		
	WO 1998-US19720	W	19980921		
AB	Topical cosmetic or pharmaceutical <b>compns. comprising</b>				

an anti-stinging effective amt. of an amino acid selected from the group consisting of an amino butyric acid, glutamine, glycine, and derivs. thereof, or mixts. thereof, as well as methods of reducing or preventing stinging using such compns. An oil-in-water emulsion contained stearic acid 2.40, glyceryl monostearate 2.20, butyl paraben 0.10, mineral oil/lanolin alc. 9.55, petrolatum/lanolin alc. 2.00, sesame oil 4.30, Pr paraben 0.10, water 72.83, triethanolamine 0.82, Me paraben 0.30, trisodium EDTA 0.10, propylene glycol 4.30, glycine 1.00%. The efficacy of the compn. in treatment of lactic acid stinging in volunteers was studied.

IT 56-12-2, .gamma.-Amino butyric acid, biological studies  
 56-40-6, Glycine, biological studies 56-85-9, Glutamine, biological studies  
 RL: BUU (Biological use, unclassified); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (topical cosmetic or pharmaceutical compns.  
 comprising anti-stinging effective amt. of amino acid)

L133 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:542693 HCAPLUS

DN 129:180125

TI Oral drug delivery compositions comprising modified amino acids and bioactive peptides

IN Sarubbi, Donald J.; Leone-Bay, Andrea; Paton, Duncan R.

PA Emisphere Technologies, Inc., USA

SO U.S., 18 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 28

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5792451	A	19980811	US 1994-205511	19940302 <--
	CA 2160693	AA	19941027	CA 1994-2160693	19940422 <--
	JP 08509474	T2	19961008	JP 1994-523595	19940422 <--
	EP 1025840	A2	20000809	EP 2000-103527	19940422 <--
	EP 1025840	A3	20000830		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	EP 1077070	A2	20010221	EP 2000-118505	19940422 <--
	EP 1077070	A3	20010523		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	US 5643957	A	19970701	US 1994-335148	19941025 <--
	US 5714167	A	19980203	US 1994-328932	19941025 <--
	US 5958457	A	19990928	US 1995-438644	19950510 <--
	US 5766633	A	19980616	US 1995-537888	19951023 <--
	US 6099856	A	20000808	US 1996-763183	19961210 <--
	US 5955503	A	19990921	US 1997-795833	19970206 <--
	US 6100298	A	20000808	US 1997-795837	19970206 <--
	US 6221367	B1	20010424	US 1997-939939	19970929 <--
	US 6071538	A	20000606	US 1997-940056	19970930 <--
	US 6245359	B1	20010612	US 1997-941616	19970930 <--
	US 2001003001	A1	20010607	US 2000-730156	20001205 <--
PRAI	US 1992-898909	B2	19920615	<--	
	US 1992-920346	A2	19920727	<--	
	US 1993-51019	A	19930422	<--	
	US 1993-59019	A2	19930422	<--	
	US 1993-76803	A2	19930614	<--	
	US 1993-143571	B2	19931026	<--	
	US 1993-168776	A2	19931216	<--	
	US 1994-205511	A	19940302	<--	
	EP 1994-916578	A3	19940422	<--	
	US 1994-231622	A2	19940422	<--	
	US 1994-231623	A2	19940422	<--	
	WO 1994-US4560	W	19940422	<--	
	US 1994-315200	A2	19940929	<--	
	US 1994-316404	A2	19940930	<--	

US 1994-328932 A2 19941025 <--  
 US 1994-335147 B2 19941025 <--  
 US 1994-335148 A3 19941025 <--  
 US 1996-17902 P 19960329 <--  
 US 1996-763183 A2 19961210 <--  
 US 1997-795837 A1 19970206 <--  
 US 1997-820694 A2 19970318 <--  
 US 1997-920346 A2 19970827 <--  
 US 1999-346970 A1 19990702

AB The present invention relates to an oral drug delivery system, and in particular to modified amino acid derivs. for use as a delivery system of sensitive agents such as bioactive peptides. The modified amino acid derivs. can form non-covalent **mixts.** with active biol. agents and in an alternate embodiment can releasably carry active agents. These **mixts.** are suitable for oral administration of biol. active agents to mammals. Methods for the prepn. of such amino acids are also disclosed.

IT 56-87-1, Lysine, biological studies 60-18-4, Tyrosine, biological studies 61-90-5, Leucine, biological studies  
 RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); RCT (Reactant); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)  
 (oral drug delivery **compns. comprising** modified amino acids and bioactive peptides)

IT 51-35-4, Hydroxyproline 52-90-4, Cysteine, biological studies 56-12-2, Gaba, biological studies 56-40-6, Glycine, biological studies 56-41-7, Alanine, biological studies 56-45-1, Serine, biological studies 56-84-8, Aspartic acid, biological studies 56-85-9, Glutamine, biological studies 56-89-3, Cystine, biological studies 60-32-2, .epsilon.-Aminocaproic acid 62-57-7, .alpha.-Aminoisobutyric acid 63-68-3, Methionine, biological studies 63-91-2, Phenylalanine, biological studies 70-26-8, Ornithine 70-47-3, Asparagine, biological studies 71-00-1, Histidine, biological studies 72-18-4, Valine, biological studies 72-19-5, Threonine, biological studies 73-22-3, Tryptophan, biological studies 73-32-5, Isoleucine, biological studies 74-79-3, Arginine, biological studies 107-95-9, .beta.-Alanine 147-85-3, Proline, biological studies 327-57-1, Norleucine 372-75-8, Citrulline 407-41-0 2835-06-5 2835-81-6, .alpha.-Aminobutyric acid 6600-40-4, Norvaline  
 RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)  
 (oral drug delivery **compns. comprising** modified amino acids and bioactive peptides)

IT 2577-90-4, Phenylalanine methyl ester  
 RL: RCT (Reactant)  
 (oral drug delivery **compns. comprising** modified amino acids and bioactive peptides)

L133 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:323132 HCAPLUS

DN 129:23447

TI A method for treating tension-type headache

IN Olesen, Jes; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf

PA Olesen, Jes, Den.; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf

SO PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	WO 9819674	A2	19980514	WO 1997-DK502	19971104 <--

W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, ES, FI, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9748632 A1 19980529 AU 1997-48632 19971104 <--  
 EP 1011656 A2 20000628 EP 1997-911150 19971104 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRAI DK 1996-1243 A 19961105 <--  
 WO 1997-DK502 W 19971104 <--

AB Tension-type headache is treated by interacting with neuronal transmission in relation to pain in connection with headache in a way which prevents or decreases sensitization of second order nociceptive neurons. In particular, treatment is performed by administration of an effective amt. of a substance which prevents or decreases central sensitization. Important examples of such substances are substances which interact with glutamate neurotransmission, such as glutamate receptor antagonists. Other examples are e.g. substances which interact with nitric oxide, such as nitric oxide synthase (NOS) inhibitors. According to a broader aspect of the invention, tension-type headache is treated by administration of substances which are effective in preventing or decreasing pain in connection with tension-type headache. An addnl. aspect of the invention relates to treatment of tension-type headache by administration of substances which substantially inhibit the activity of NOS. Evidence for central sensitization in chronic myofascial pain, as well as mechanisms of spontaneous tension-type headaches, are also described. **Gabapentin** and dextromethorphen had a prophylactic effect on chronic tension-type headaches.

IT 56-86-0, L-Glutamic acid, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (glutamate prodn. and release and action; tension-type headache treatment)

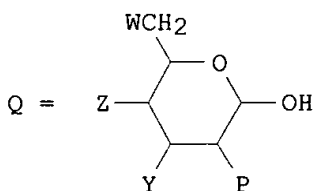
IT 56-12-2, GABA, biological studies 56-40-6, Glycine, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (prodn. and release and action; tension-type headache treatment)

IT 56-12-2D, .gamma.-Aminobutyric acid, derivs. 56-40-6D, Glycine, derivs. 74-79-3D, L-Arginine, derivs. 372-75-8D, Citrulline, derivs. 2149-70-4 2149-70-4D, derivs. 2835-06-5D, derivs. 17035-90-4 17035-90-4D, derivs. 22059-21-8 22059-21-8D, derivs. 50903-99-6, L-NAME 50903-99-6D, L-NAME, derivs. 60142-96-3, **Gabapentin** 60142-96-3D, **Gabapentin**, derivs.  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (tension-type headache treatment)

L133 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1996:483546 HCAPLUS  
 DN 125:143306  
 TI Preparation of mono- and dicarboxylic acid amides with amino acids or glycosamines as selectively active cannabinoid peripheral receptor agonists  
 IN Della Valle, Francesco; Leon, Alberta; Marcolongo, Gabriele; Lorenzi, Silvana  
 PA Lifegroup S.P.A., Italy  
 SO PCT Int. Appl., 77 pp.  
 CODEN: PIXXD2

DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9618600	A1	19960620	WO 1995-EP4926	19951213 <--
	W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2207804	AA	19960620	CA 1995-2207804	19951213 <--
	AU 9643441	A1	19960703	AU 1996-43441	19951213 <--
	EP 799188	A2	19971008	EP 1995-942141	19951213 <--
	EP 799188	B1	19990915		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 11501615	T2	19990209	JP 1995-518264	19951213 <--
	AT 184591	E	19991015	AT 1995-942141	19951213 <--
PRAI	IT 1994-MI2513		19941214 <--		
	WO 1995-EP4926		19951213 <--		
OS	MARPAT 125:143306				
GI					



AB Title carboxylic acid amides R1CONR1R2 [R1 = linear or branched C9-13 alkyl, optionally contg. one double bond, optionally contg. one or more OH groups, R4CONR5R6, R4CO2R7; R4 = linear or branched C8-22 alkyl, optionally contg. one double bond, optionally substituted with one or more linear or branched C1-8 alkyl groups and/or one or more OH groups; NR2, NR5 = independently optically active or nonactive .alpha.-amino acid contg. aliph. or arylaliph. side chain optionally substituted with OH, OPO3H2, OP(O)(OH)OCH2CH(OH)CH2OH, SH, SMe; a .beta.- or an optionally methylated or ethylated .gamma.-amino acid contg. and aliph. or arylaliphatic side chain; or a glycosamine residue Q with one of the groups P, W, Y, Z being N(R3)COR1 and the others being independently H, OH; R3, R6 = independently H, Me; R7 = H, linear or branched C1-20 alkyl], and pharmaceutical **compns.** contg. them for modulation of cannabinoid peripheral receptors are described. Thus, Me(CH2)14CO-L-Ser-OH, prepd. in 89% yield via acylation of L-Ser with palmitoyl chloride in aq. K2CO3, showed 100% displacement of [3H]-WIN 55,212-2 in a cannabinoid receptor membrane assay.

IT 51-35-4, 4-Hydroxy-L-proline 52-90-4, L-Cysteine, reactions 56-12-2, .gamma.-Aminobutyric acid, reactions 56-40-6, Glycine, reactions 56-45-1, L-Serine, reactions 107-95-9, .beta.-Alanine 5680-79-5, Glycine methyl ester hydrochloride 5680-80-8, L-Serine methyl ester hydrochloride

RL: RCT (Reactant)

(prepn. of mono- and bicarboxylic acid amides with amino acids or glycosamines as selectively active cannabinoid peripheral receptor agonists)

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L157 ANSWER 1 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2001-388393 [41] WPIX

CR 1992-216971 [26]; 1993-386441 [48]; 1996-464187 [46]; 1997-144377 [13];  
1997-177956 [16]; 1998-040695 [04]; 1998-129310 [12]; 1999-119283 [10];  
2000-194861 [17]; 2000-655473 [54]; 2001-040317 [64]

DNC C2001-118436

TI Treatment of e.g. seizure disorders, Huntington's disease, Parkinson's  
disease, cerebral ischemia, spasticity, depression and psychosis by  
administering **4-amino-3-(2-methylpropyl)**  
**butanoic acid**.

DC B05

IN ANDRUSZKIEWICZ, R; SILVERMAN, R B

PA (NOUN) UNIV NORTHWESTERN

CYC 1

PI US 6197819 B1 20010306 (200141)\* 16p A61K031-195 <--

ADT US 6197819 B1 CIP of US 1990-618692 19901127, CIP of US 1992-886080  
19920520, Cont of US 1993-64285 19930518, US 1995-420905 19950411

PRAI US 1993-64285 19930518; US 1990-618692 19901127; US 1992-886080  
19920520; US 1995-420905 19950411

IC ICM **A61K031-195**

AB US 6197819 B UPAB: 20010724

NOVELTY - **4-amino-3-(2-methylpropyl)**

**butanoic acid** (Ia) and its salts are new.

ACTIVITY - Anticonvulsant; antidepressant; anxiolytic;  
neuroprotective; cerebroprotective; neuroleptic.

**4-amino-3-(2-methylpropyl)**

**butanoic acid** (Ia) had an ED50 for the **gabapentin**  
receptor of 0.044 micro M.

MECHANISM OF ACTION - Increases brain neuronal GABA.

USE - For treatment of seizure disorders, Huntington's disease,  
Parkinson's disease, cerebral ischemia, spasticity, depression, anxiety  
and psychosis in mammals.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B10-B02J; B14-F02D1; B14-J01A1; B14-J01A3; B14-J01A4; B14-J01B3;  
B14-J01B4; B14-J05A; B14-J05D; B14-J07

TECH UPTX: 20010724

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) are prepared by  
reduction of a corresponding azide e.g. an azide of formula (II) is  
reduced to give (Ia).

L157 ANSWER 2 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2001-040317 [05] WPIX

CR 1992-216971 [26]; 1993-386441 [48]; 1996-464187 [46]; 1997-144377 [13];

1997-177956 [16]; 1998-040695 [04]; 1998-129310 [12]; 1999-119283 [10];  
 2000-194861 [17]; 2000-655473 [54]; 2001-388393 [20]

DNC C2001-011567

TI New method of treating seizure disorders and other CNS disorders.

DC B05

IN ANDRUSZKIEWICZ, R; SILVERMAN, R B; YUEN, P

PA (NOUN) UNIV NORTHWESTERN; (WARN) WARNER LAMBERT CO

CYC 1

PI US 6140366 A 20001031 (200105)\* 14p A61K031-195 <--

ADT US 6140366 A CIP of US 1990-618692 19901127, CIP of US 1992-886080  
 19920520, Cont of US 1993-64285 19930518, Div ex US 1995-420905 19950411,  
 Div ex US 1997-899918 19970724, US 1999-244306 19990204

PRAI US 1993-64285 19930518; US 1990-618692 19901127; US 1992-886080  
 19920520; US 1995-420905 19950411; US 1997-899918 19970724; US  
 1999-244306 19990204

IC ICM A61K031-195

AB US 6140366 A UPAB: 20010724

NOVELTY - Method of treating a patient with cerebral ischemia comprising  
 administration of 1-300 mg/kg of (R-(-)) or S-(+) 4-  
**amino-3-(2-methylpropyl)butanoic acid**, is new.

ACTIVITY - Cerebroprotective; antiparkinsonian; anticonvulsant;  
 nootropic; antidepressant; anxiolytic; antipsychotic; vasotropic; .

MECHANISM OF ACTION - GAD activator.

USE - The method is useful in the treatment of cerebral ischemia  
 (claimed), but could also be useful in the treatment of CNS disorders such  
 as epilepsy, Huntington's Chorea, Parkinson's disease, tardive dyskinesia  
 and spasticity, and possibly as antidepressant, anxiolytic and  
 antipsychotic treatment.

ADVANTAGE - The compounds activate GAD in vitro and have a  
 dose-dependent protective effect on seizure in vivo. In assays, it was  
 found that the S-(+) enantiomer of **4-amino-3**  
**-(2-methylpropyl)butanoic acid** (IBG) potently displaced  
 tritiated **gabapentin** from a novel high-affinity site in rat  
 brain membrane fractions (IC50 of 0.044  $\mu$ M, cf. 0.86, 0.10 and 0.14  $\mu$ M  
 for (R)-IBG, ( plus or minus )-IBG and **gabapentin** respectively).  
 The S-(+)-enantiomer was responsible for all blockade of maximal  
 electroshock seizures in mice and rats.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B10-B02J; B14-J01A1; B14-J01A3; B14-J01B3; B14-J01B4

L157 ANSWER 3 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2000-105566 [09] WPIX

DNC C2000-031623

TI New composition containing butanoic acid derivatives as tablets or  
 granules.

DC B05

IN AOMATSU, A

PA (WARN) WARNER LAMBERT CO

CYC 78

PI WO 9959572 A1 19991125 (200009)\* EN 99p A61K031-195 <--

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SL SZ UG ZW

W: AE AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KP  
 KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US  
 UZ VN YU ZA

AU 9940733 A 19991206 (200019) A61K031-195 <--

JP 2000034227 A 20000202 (200021) 34p A61K031-195 <--

BR 9910494 A 20010109 (200106) A61K031-195 <--

NO 2000005765 A 20001114 (200113) A61K031-195 <--

EP 1077691 A1 20010228 (200118) EN A61K031-195 <--

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI

ADT WO 9959572 A1 WO 1999-US10186 19990510; AU 9940733 A AU 1999-40733  
 19990510; JP 2000034227 A JP 1999-133769 19990514; BR 9910494 A BR



1999-10494 19990510, WO 1999-US10186 19990510; NO 2000005765 A WO  
 1999-US10186 19990510, NO 2000-5765 20001114; EP 1077691 A1 EP 1999-924164  
 19990510, WO 1999-US10186 19990510  
 FDT AU 9940733 A Based on WO 9959572; BR 9910494 A Based on WO 9959572; EP  
 1077691 A1 Based on WO 9959572  
 PRAI JP 1998-133112 19980515  
 IC ICM **A61K031-195**  
 ICS A61K009-14; A61K009-16; A61K009-48; A61K031-00; A61K047-10;  
 A61K047-14; A61K047-18  
 ICA C07C229-28  
 AB WO 9959572 A UPAB: 20010110

NOVELTY - A sterilized solid composition containing **4-amino-3-substituted-butanoic** acid derivative

(I), a humectant and an auxiliary agent if needed, is new.

DETAILED DESCRIPTION - A sterilized solid composition containing **4-amino-3-substituted-butanoic** acid derivative of formula (I), a humectant and an auxiliary agent if needed, is new.

R1 = hydrogen atom, hydroxyl, methyl or an ethyl group;

R2 = monovalent group selected from mono- or di-substituted 3-8C alkyl or 3-8C alkylene, mono-, di- or tri-substituted 3-8C cycloalkyl, condensed ring group formed by ortho-fusion of a mono-, di- or tri-substituted phenyl ring with 4-8C or 5-8C cycloalkyl, alkyl 3-8C cycloalkyl linked to 1-4C alkylene (optionally interrupted with -O-, -S-, -SS or mono-, di- or tri-substituted 5-8C cycloalkyl where (-CH2) is replaced by -O-, -NH-, -S-, -SO- or -S(O)2, 5-8C cycloalkenyl or cycloalkanedieryl group where (-CH2) is mono- or di-substituted, alkyl, 5-8C cycloalkyl linked to 1-4C alkylene (optionally mono-, di- or tri-substituted (-CH2) replaced by -O-, -NH-, -S-, -SO- or -S(O)2, optionally mono-, di- or tri-substituted phenyl or naphthyl), alkylphenyl group (optionally mono-, di- or tri-substituted and linked to 1-4C alkylene);

R1 and R2 together with the carbon atom to which they are attached, may form a divalent group with mono-, di-, tri- or tetra-substituted 5-8C cycloalkylidene, condensed group formed by ortho-fusion of mono-, di-, tri- or tetra-substituted phenyl ring with 4-8C cycloalkylidene.

An INDEPENDENT CLAIM is also included for the preparation of a solid composition containing the **4-amino-3-substituted butanoic** acid derivative (I) as defined above, a humectant and an auxiliary agent.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - A stabilized solid composition in the form of tablets, powders, granules or capsules (claimed).

ADVANTAGE - Lactam formation during formulation and storage which leads to degradation of the product is prevented by blocking evaporation and movement of residual water by addition of the humectant. The formulation showed increased dissolution and high stability (disclosed).  
 Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-H; B07-H; B10-A04; B10-A07; B10-B01; B10-B02B; B10-E04C; B12-M11; B14-C01; B14-J01; B14-J07

TECH UPTX: 20000218

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Humectant: 0.01-25% of ethylene glycol, propylene glycol, butylene glycol, sorbitol, glycerol and/or aliphatic acid ester, preferably sorbitol is used as the humectant. 0.1-50% humectant is used for film coated tablets.  
 Preferred Preparation: Specific amount of (I) is taken and fluidised by fluidised granulation method where a stabilizer (humectant) is sprayed into the powders. The stabilizer is added as a solution, dissolved in water or organic solvent, whereby a small amount is sufficient for uniformly adhering into the powder surface of (I). (I) is combined if necessary with an auxiliary agent, neutral amino acid, binders and sweetening agents. The granules are compressed to form tablets and surface coated if necessary.

Preferred Amino Acid: L-leucine, L-isoleucine, L-valine, L-alanine, D-leucine, D-isoleucine, D-valine, D-alanine, DL-leucine, DL-isoleucine, DL-valine, DL-alanine and/or glycine is used as the amino acid in the composition.

L157 ANSWER 4 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2000-086571 [07] WPIX

DNC C2000-024063

TI Stabilized pharmaceutical composition containing **4-amino-3-substituted butanoic** acid derivative, used for treating cerebral diseases and neurodegenerative disorders.

DC B05

IN AOMATSU, A

PA (WARN) WARNER LAMBERT CO

CYC 78

PI WO 9959573 A1 19991125 (200007)\* EN 114p A61K031-195 <--  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SL SZ UG ZW  
 W: AE AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KP  
 KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US  
 UZ VN YU ZA

JP 2000034226 A 20000202 (200017) 40p A61K031-195 <--

AU 9940735 A 19991206 (200019) A61K031-195 <--

BR 9910508 A 20010102 (200104) A61K031-195 <--

NO 2000005768 A 20001114 (200109) A61K000-00

EP 1077692 A1 20010228 (200113) EN A61K031-195 <--

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI

ADT WO 9959573 A1 WO 1999-US10190 19990510; JP 2000034226 A JP 1999-133773  
 19990514; AU 9940735 A AU 1999-40735 19990510; BR 9910508 A BR 1999-10508  
 19990510, WO 1999-US10190 19990510; NO 2000005768 A WO 1999-US10190  
 19990510, NO 2000-5768 20001114; EP 1077692 A1 EP 1999-924166 19990510, WO  
 1999-US10190 19990510

FDT AU 9940735 A Based on WO 9959573; BR 9910508 A Based on WO 9959573; EP  
 1077692 A1 Based on WO 9959573

PRAI JP 1998-133113 19980515

IC ICM A61K000-00; **A61K031-195**

ICS A61K009-16; A61K009-20; A61K047-16; A61K047-18; **A61P025-00;**

**A61P025-28**

ICA A61K009-08; A61K009-14

AB WO 9959573 A UPAB: 20000209

NOVELTY - Stabilized pharmaceutical composition contains a **4-amino-3-substituted butanoic** acid derivative  
 (I) and an alpha -**amino** acid.

DETAILED DESCRIPTION - Pharmaceutical composition contains a  
**4-amino-3-substituted butanoic** acid  
 derivative (I), an alpha -**amino** acid and optionally an auxiliary  
 agent.

R1 = H, OH, methyl or ethyl;

R2 = 3-8C alkyl (optionally substituted by 1 or 2 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carbalkoxy), 3-8C alkylene, condensed ring formed by ortho-fusion of phenyl (optionally substituted by 1-3 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, carboxy or carbalkoxy) with 4-8C cycloalkyl, 5-8C cycloalkenyl or 5-8C cycloalkanedieryl, alkyl 3-8C cycloalkyl linked through cycloalkyl to 1-4C alkylene optionally interrupted by O, S or SS (with cycloalkyl optionally substituted by 1-3 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carbalkoxy), 5-8C cycloalkyl with one CH2 replaced by O, NH, S, SO or SO2 (with 1 or 2 unsubstituted CH2 optionally substituted by 1 or 2 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carbalkoxy), 5-8C cycloalkenyl or cycloalkanedieryl with 1 CH2 replaced by O, NH, N, S, SO or SO2 (with 1 or 2 unsubstituted CH2 optionally substituted by 1 or 2 halo, CF3, OH, alkyl, alkoxy, alkylthio, NH2, NO2, oxo, carboxy or carbalkoxy), a condensed ring formed by ortho fusion of phenyl with 5-8C cycloalkyl with 1 CH2 replaced by O, NH, S, SO or SO2 (with phenyl optionally substituted by 1 or 2 halo, CF3, OH, alkyl,

alkoxy, alkylthio, NH<sub>2</sub>, NO<sub>2</sub>, carboxy or carboalkoxy), a condensed ring formed by ortho fusion of phenyl with 5-8C cycloalkenyl or cycloalkanedienyl with 1 CH<sub>2</sub> replaced by O, NH, N, S, SO or SO<sub>2</sub> (with phenyl optionally substituted by 1 or 2 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, alkylthio, NH<sub>2</sub>, NO<sub>2</sub>, carboxy or carboalkoxy), alkyl 5-8C cycloalkyl with the cycloalkyl linked to 1-4C alkylene optionally interrupted by O, S or SS and 1 CH<sub>2</sub> replaced by O, NH, S, SO or SO<sub>2</sub> (with 1 or 2 unsubstituted CH<sub>2</sub> optionally substituted by 1-3 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, alkylthio, NH<sub>2</sub>, NO<sub>2</sub>, oxo, carboxy or carboalkoxy), phenyl (optionally substituted by methylenedioxy) or phenyl or naphthyl (optionally substituted by 1-3 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, amino, NO<sub>2</sub>, carboxy, phenoxy, phenylmethoxy (optionally phenyl substituted by halo, CF<sub>3</sub>, alkoxy, NH<sub>2</sub>, NO<sub>2</sub>, carboxy or carboalkoxy) or 5-8C cycloalkylmethoxy with 1 CH<sub>2</sub> optionally replaced by O, NH, S, SO or SO<sub>2</sub> (optionally ring substituted by halo, CF<sub>3</sub>, OH, OH, alkyl, alkoxy, NH<sub>2</sub>, NO<sub>2</sub>, carboxy or carboalkoxy) or 5-8C cycloalkenylmethoxy or 5-8C cycloalkanedienylmethoxy both with 1 CH<sub>2</sub> optionally replaced by O, NH, N, S, SO or SO<sub>2</sub> (optionally substituted by halo, CF<sub>3</sub>, OH, alkyl, alkoxy, NH<sub>2</sub>, NO<sub>2</sub>, oxo, carboxy or carboalkoxy)), 1-4C alkylphenyl, alkoxyphenyl, thiophenyl or SS-phenyl (all phenyl linked to 1-4C alkylene via O, S or SS, optionally interrupted by O, S or SS and optionally substituted by 1-3 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, NH<sub>2</sub>, NO<sub>2</sub> or carboxy) or oxyphenyl, thiophenyl or SS-phenyl (all optionally substituted by 1-3 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, NH<sub>2</sub>, NO<sub>2</sub> or carboxy) or diphenylamino or

CR1R2 = 5-8C cycloalkylidene (optionally substituted by 1-4 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, alkylthio, cycloalkyl, phenyl, NH<sub>2</sub>, NO<sub>2</sub> or carboxy), with 1 CH<sub>2</sub> optionally replaced by O, NH, S, SO or SO<sub>2</sub> and at least 1 unsubstituted CH<sub>2</sub> optionally substituted by 1-4 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, alkylthio, NH<sub>2</sub>, NO<sub>2</sub>, carboxy or carboalkoxy, 5-8C cycloalkenylidene or 5-8C cycloalkanedienylidene (both optionally substituted by 1-4 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, alkylthio, cycloalkyl, phenyl, NH<sub>2</sub>, NO<sub>2</sub>, oxo, carboxy or carboalkoxy), with 1 CH<sub>2</sub> optionally replaced by O, NH, S, SO or SO<sub>2</sub> and at least 1 unsubstituted CH<sub>2</sub> optionally substituted by 1-4 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, alkylthio, NH<sub>2</sub>, NO<sub>2</sub>, oxo, carboxy or carboalkoxy or a condensed ring formed by ortho fusion of phenyl with 4-8C cycloalkylidene, 5-8C cycloalkenylidene or cycloalkanedienylidene (all optionally phenyl substituted by 1-4 halo, CF<sub>3</sub>, OH, alkyl, alkoxy, alkylthio, NH<sub>2</sub>, NO<sub>2</sub>, carboxy or carboalkoxy).

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - For treating cerebral disorders such as epilepsy, hypokinesia, cranial traumas and for treating neurodegenerative disorders such as Alzheimer's disease, Huntington's chorea or Parkinson's disease and amyotrophic lateral sclerosis. The composition is used for improving cerebral functions in senile patients.

ADVANTAGE - Lactam formation through the intramolecular condensation is prevented by blocking both the amino group and carbonyl group of (I) by adding an butanoic acid derivative and adding an amino acid as a stabilizer so that the composition has good storage stability.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B10-B02; B14-J01A3; B14-J01A4; B14-J07; B14-N16; B14-S01

TECH UPTX: 20000209

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: The total amount of alpha-amino acid is 0.001-80 moles per mole of (I).

The acidic alpha-amino acid is used in the form of the corresponding alkali salt acid amide, alkyl-substituted derivative of acid amide or their alkyl esters.

The basic alpha-amino acid is used in the form of the corresponding acid addition salt or monoacylated derivative. The acidic alpha-amino acid and basic alpha-amino acid are also used in the form of corresponding acidic amino acid-basic amino acid adduct.

The composition contains gabapentin, pregabalin,

**baclofen**, 3-aminomethyl-4-cyclohexyl-butanoic acid,  
3-aminomethyl-5-cyclohexyl pentanoic acid, 3-aminomethyl-4-phenyl-  
butanoic acid or 3-aminomethyl-5-phenyl-pentanoic acid.

L157 ANSWER 5 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1984-271746 [44] WPIX  
DNC C1984-114961  
TI Seizure-controlling compsns. contg. GABA-T inhibitor - with glycine,  
sarcosine or N,N-di methyl glycine synergist.  
DC B05 P33  
IN SARHAN, S; SEILER, N  
PA (RICH) MERRELL DOW PHARM INC; (LTOR) MERRELL TORAUDE & CIE; (LTOR) MERRELL  
TORAUDE & CIE  
CYC 19  
PI GB 2138680 A 19841031 (198444)\* 11p  
EP 124091 A 19841107 (198445) EN  
R: AT BE CH DE FR GB IT LI LU NL SE  
AU 8426443 A 19841101 (198451)  
JP 59206309 A 19841122 (198502)  
DK 8402134 A 19841030 (198505)  
PT 78492 A 19841220 (198507)  
ZA 8403032 A 19841017 (198508)  
US 4540582 A 19850910 (198539)  
GB 2138680 B 19860521 (198621)  
US 4595697 A 19860617 (198627)#  
CA 1228818 A 19871103 (198748)  
IL 71650 A 19880731 (198846)  
EP 124091 B 19891220 (198951) EN  
R: AT BE CH DE FR IT LI LU NL SE  
DE 3480764 G 19900125 (199005)  
JP 05027606 B 19930421 (199319) 10p A61K031-195 <--  
ADT GB 2138680 A GB 1984-10504 19840425; EP 124091 A EP 1984-104705 19840426;  
JP 59206309 A JP 1984-84236 19840427; ZA 8403032 A ZA 1984-3032 19840424;  
US 4540582 A US 1984-594079 19840328; GB 2138680 B GB 1984-10504 19840425;  
US 4595697 A Div ex US 1984-594079 19840328, US 1985-705955 19850227; JP  
05027606 B JP 1984-84236 19840427  
FDT US 4595697 A Div ex US 4540582; JP 05027606 B Based on JP 59206309  
PRAI GB 1983-11804 19830429; US 1985-705955 19850227  
REP A3...8740; FR 2437834; GB 2120244; No-SR.Pub; US 3960927  
IC A61J031-24; A61K031-19; A61K045-06; C07C101-04  
ICM **A61K031-195**  
ICS A61J031-24; A61K031-19; A61K031-22; A61K045-06; C07C101-04  
AB GB 2138680 A UPAB: 19971113  
Compsn. comprises (a) a GABA-T inhibitor (I), (b) glycine, sarcosine or  
N,N-dimethylglycine, or its 1-8C alkyl ester or pharmaceutically  
acceptable salt, and (c) a carrier or diluent. Pref. (I) is gamma-vinyl  
GABA, esp. the (s)-isomer free from (R)-isomer; 4-amino-hepta-5,6-dienoic  
acid; gamma-acetylenic GABA; aminooxyacetic acid ethanolamine o-sulphate;  
gabaculine; isogabaculine; or their salts.  
USE/ADVANTAGE - For treating both convulsive and non-convulsive  
seizures associated with e.g. epilepsy, trauma, alcohol withdrawals, drug  
withdrawal, tetanus, metabolic disease, hyperthermia, drug induction and  
porphyria. The amino acid (b) gives synergistic effects in seizure  
control, permitting a reduction in the dosage of (I) or permitting greater  
control at the same dosage. Dose of (I) may be reduced by a factor of  
2-5, so that daily dose is 0.2-2 g. p.o. Amt. of (b) is 2-12 g/day, pref.  
3-4 g/day.  
Dwg.0/0  
FS CPI GMPI  
FA AB  
MC CPI: B10-A09A; B10-A18; B10-B02J; B12-C09; B12-D04; B12-G01  
ABEQ EP 124091 B UPAB: 19930925

A pharmaceutical composition for controlling seizures in a patient in need  
thereof which comprises: (a) gamma-vinyl GABA, or a pharmaceutically  
acceptable salt thereof, and (b) glycine, sarcosine, or N,N -  
dimethylglycine, or a C1-C8 alkyl ester thereof, or a pharmaceutically

acceptable salt thereof, in a synergistically effective ratio, and (c) a pharmaceutically acceptable carrier or diluent.

ABEQ GB 2138680 B UPAB: 19930925

A pharmaceutical composition for controlling seizures in a patient in need thereof which comprises: (a) a GABA-T inhibitor (as hereinbefore defined) (b) glycine, sarcosine, or N,N-dimethylglycine, or a C1-C8 alkyl ester thereof, or a pharmaceutically acceptable salt thereof, and (c) a pharmaceutically acceptable carrier or diluent.

ABEQ US 4540582 A UPAB: 19930925

Pharmaceutical compsn. comprises 4-vinyl-4-aminobutyric acid (I) or its nontoxic salts (dosage 0.2-2.0 g/day); glycosine, sarcosine or N,N-dimethylglycine or their nontoxic salts or esters (dosage 2-12 g/day); and the usual carriers and additives. Glycine, sarcosine or N,N-dimethylglycine have a synergistic effect on the neurotransmitter inhibiting action of (I) on the central nervous system.

USE - The prods. are improved therapeutic agents for the treatment of convulsive and non-convulsive seizures, esp. epilepsy, trauma, drug withdrawal, tetanus, etc.

ABEQ US 4595697 A UPAB: 19930925

New method for controlling seizures comprises admin. of a 0.2-2 g/day of gamma-vinylGABA (GVG) or its salts and b 2-12 g/day of 1-8C alkyl ester of glycine, sarcosine, N,N-dimethylglycine or salt. Pref. GVG is S isomer S.G.VG. Dosage unit for controlling seizures is a 50-100 mg of GVG or salts; b 250-500 mg 1-8C alkyl ester of glycine, sarcosine, N,N-dimethylglycine or salt and ca carrier or diluent.

ADVANTAGE - S.GVG (4-amino-hex-5-anoic acid) is selective enzyme-activated irreversible inhibitor of GABAtransaminase (GABA-T) which by blocking catabolism of GABA in CNS allows its conc. to rise and so inhibit CNS neurotransmission. S.GVG is used at half concn. of S.R.GVG in treatment of seizure disorders, esp. epilepsy. Effect is synergistically increased 2-5 times by glycine etc. are also synergistic with GABA-T inhibitors other than GVG.

ABEQ JP 93027606 B UPAB: 19931113

Compsn. comprises (a) a GABA-T inhibitor (I), (b) glycine, sarcosine or N,N-dimethylglycine, or its 1-8C alkyl ester or pharmaceutically acceptable salt, and (c) a carrier or diluent. Pref. (I) is gamma-vinyl GABA, esp. the (s)-isomer free from (R)-isomer; 4-amino-hepta-5,6-dienoic acid; gamma-acetylenic GABA; aminooxyacetic acid ethanolamine o-sulphate; gabaculine; isogabaculine; or their salts.

USE/ADVANTAGE - For treating both convulsive and non-convulsive seizures associated with e.g. epilepsy, trauma, alcohol withdrawals, drug withdrawal, tetanus, metabolic disease, hyperthermia, drug induction and porphyria. The amino acid (b) gives synergistic effects in seizure control, permitting a reduction in the dosage of (I) or permitting greater control at the same dosage. Dose of (I) may be reduced by a factor of 2-5, so that daily dose is 0.2-2 g. p.o. Amt. of (b) is 2-12 g/day, pref. 3-4 g/day. (J59206309-A)

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(FILE 'HOME' ENTERED AT 11:22:43 ON 12 AUG 2001)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 11:22:57 ON 12 AUG 2001

E WO9959573/PN  
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E WO99-US10190/AP, PRN  
L2 1 S E3, E4  
E JP98-133113/AP, PRN  
L3 1 S E4  
L4 1 S L1-L3  
E AOMATSU A/AU  
L5 4 S E4  
L6 4 S L4, L5  
SEL RN